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Linda Pestano

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT

PAPER NUMBER

1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

02/22/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/770,257	Applicant(s) PESTANO, LINDA	
	Examiner Anne Marie S. Wehbe	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 7-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 15-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 2/2/04 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response to the restriction requirement received on 10/13/06 has been entered. Applicant's election with traverse of the subject matter of Group II is acknowledged. Claims 1-22 are pending in the instant application. Claims 7-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/13/06. Claims 1-6 and 15-22 are therefore under examination at this time. An action on the merits follows.

Election/Restrictions

As noted above, the applicant elected with traverse Group II in the reply filed on 10/13/06. However, since the applicant did not provide any specific arguments traversing the grounds for restriction, the traversal is not found persuasive.

The requirement is therefore still deemed proper and is made FINAL.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application for the following Figures: 3A, 3B, 3C, 4A, 4B, 5, 6A, and 9B. While the graphs show bars of distinct shades, the legend boxes identifying which color is which are illegible such that it

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is unclear what each shade of bar represents. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

Replacement Drawing Sheets

Drawing changes must be made by presenting replacement sheets which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be presented either in the drawing amendments section, or remarks, section of the amendment paper. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). A replacement sheet must include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of the amended drawing(s) must not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and within the top margin.

Annotated Drawing Sheets

A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be submitted or required by the examiner. The annotated drawing sheet(s) must be clearly labeled as "Annotated Sheet" and must be presented in the amendment or remarks section that explains the change(s) to the drawings.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

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If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mature dendritic cells derived from monocytic dendritic precursor cells cultured in GM-CSF and IL-15 that exhibit increased expression of CD80 and CD86 as compare to mature dendritic cells cultured in the presence of GM-CSF and IL-4 and are capable of increasing the proliferation of NK cells in culture by at least 10 fold or at least 30 fold after at least 7 days of co-culture, does not reasonably provide enablement for any dendritic cell with the claimed phenotypes of increased expression of CD80 and CD86 as compare to mature dendritic cells cultured in the presence of GM-CSF and IL-4 and the capacity to increasing the proliferation of NK cells in culture by at least 10 fold or at least 30 fold after at least 7 days of co-culture. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to dendritic cells with the following phenotype: increased expression of CD80 and CD86 as compared to mature dendritic cells cultured in the presence of GM-CSF and IL-4 and the capacity to increasing the proliferation of NK cells in culture by at least 10 fold or at least 30 fold after at least 7 days of co-culture. However, the specification clearly demonstrates only mature dendritic cells produced by culture of low adherence monocytic dendritic cell precursors in the presence of GM-CSF and IL-15 have the recited characteristics of increased levels of CD80 and CD86 as compared to mature dendritic cells cultured in GM-CSF and IL-4, and the ability to induce a 10-30 fold increase in the number of NK cells in a co-culture of dendritic cells and NK cells after seven days. Working example 1 clearly demonstrates that only mature dendritic cells produced by culturing low-adherence dendritic cell precursors in GM-CSF and IL-15 expressed increased levels of CD86 and CD80 compared to mature or immature dendritic cells produced by culture in GM-CSF and IL-4. Table 1 on page 18 shows that the immature dendritic cells produced by culture in GM-CSF and IL-15 did not express increased levels of CD86 and CD80. Further, example 5 in the specification demonstrates that immature dendritic cells produced by culture in GM-CSF and IL-15 were not capable of inducing significant expansion of NK cells in co-culture (specification, page 21, Table 3). Specifically, the specification states, “[o]nly matured DCs generated in GM-CSF and IL-15 were able to expand NK cells to a significant degree” (specification, page 21, lines 13-14). Thus, the specification clearly demonstrates in the working examples that it is the mature dendritic cells, not immature dendritic cells, that exhibit the claimed phenotype.

Furthermore, the specification fails to provide any guidance as to alternative culture conditions for producing immature or mature dendritic cells that share the same phenotype as the

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mature dendritic cells produced by culture of low-adherence dendritic precursor cells in GM-CSF and IL-15. The specification also fails to provide any guidance as to whether dendritic cells with the claimed phenotype can be isolated from any mammal, or under what conditions or isolation techniques. It is further noted that while the prior art teaches various methods for culturing dendritic precursor cells to produce immature and mature dendritic cells, including culture in GM-CSF and IL-13, the prior art does not teach that these dendritic cells exhibit increased CD80 and CD86 compared to dendritic cells cultured in GM-CSF and IL-4, or that these cells can induce significant NK cell expansion in in vitro co-culture. Thus, based the state of art at the time of filing, the lack of guidance in the specification for methods or techniques for producing or isolating dendritic cells with the claimed phenotype other than culture of low-adherence dendritic precursor cells in GM-CSF and IL-15 and further inducing their maturation, the demonstration in the working examples that immature dendritic cells produced by culture of low-adherence dendritic precursor cells in GM-CSF and IL-15, do not share this phenotype, and the breadth of the claims, it would have required undue experimentation to identify and develop alternative techniques to produce or isolate dendritic cells with the claimed phenotype and use them in the claimed methods of inducing the activation or proliferation of NK cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 4-5, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 depends on claim 1. Claim 4 recites the dendritic cell of claim 1, “wherein the number of NK cells is increased by at least 10 fold from the initial NK cell numbers after at least seven days in co-culture. Claim 1 is a product claim that simply characterizes the dendritic cell as on the “can induce the activation and proliferation of natural killer cells”. There is insufficient antecedent basis for “the number of NK cells” in claim 1. Note that “natural killer” in claim 1 is not followed by any abbreviation. Further, there are no actual NK cells in the product of claim 1. Claim 1 is directed to dendritic cells, not a culture or co-culture of dendritic cells and NK cells. It is further noted that the “co-culture” recited in claim 4 is confusing as there is no culturing step or culture claimed and the elements of the “co-culture” are not defined. If the limitation of claim 4 is intended to represent a phenotype of the cell, it is suggested that the claim be amended to recite “The dendritic cell according to claim 1, wherein the dendritic cell is capable of increasing by at least 10 fold the number of NK cells present in a co-culture of NK cells and said dendritic cells after at least seven days of co-culture from the initial number of NK cells present in said co-culture.”

Claim 5 is also indefinite in its recitation of “the number of NK cell”. As noted above, there is no antecedent basis for “NK cell” or “number of NK cell” in claim 1. Further the recitation in claim 5, “wherein the number of NK cell is increased by at least 30 fold” is confusing and indefinite as there is no indication of under what conditions the NK cell number increases or any reference level of NK cells for the “30 fold” increase.

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Claims 15-22 are unclear and indefinite in that they encompass contact between the NK cells and dendritic cells *in vivo*, see dependent claim 19 in particular. For *in vivo* contact, the claims are confusing in that no active steps for administering either a population of dendritic cells and/or a population of NK cells to a mammal are recited in the claims. Thus, it is unclear whether the hand of man is actually part of the *in vivo* method, as mammals naturally comprise dendritic cells and NK cells, and these cells naturally come into contact with each other. As such the metes and bounds of the claims cannot be determined.

Claim 22 recites the method of claim 21 “wherein the population of leukocytes are further contacted with antigen presenting dendritic cells”. It is unclear whether these dendritic cells are different from the dendritic cell with which the NK cell is contacted in the base claim, claim 15.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Mohamadzadeh et al. (2001) J.Exp. Med. 194:1013-1019. Mohamadzadeh et al. teaches the preparation of immature dendritic cells by culturing monocytes in the presence of either GM-CSF and IL-15 or GM-CSF and IL-4 (Mohamadzadeh et al., pages 1013-1014). Mohamadzadeh et al. further teaches maturation of the dendritic cells by treatment with LPS (Mohamadzadeh et al., page 1014). Mohamadzadeh et al. teaches that the mature dendritic cells produced from the culture of monocytic precursors in GM-CSF and IL-15 exhibited expression of CD1a, and high levels of CD80 and CD86 (Mohamadzadeh et al., page 1015). While Mohamadzadeh et al. did not do a direct comparison of the phenotype of the IL-15 dendritic cells with the IL-4 dendritic cells, it is noted that the IL-15 dendritic cells of Mohamadzadeh et al. were produced using the same culture conditions, i.e. culture in IL-15 and GM-CSF, and appear to express the same markers. It is also noted that while Mohamadzadeh et al. did not test the ability of these cells to induce the proliferation or activation of NK cells, "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). Further, the applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923

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(BPAI 1989). Thus, by teaching mature dendritic cells produced from the culture of monocytic precursor cells in IL-15 and GM-CSF, Mohamadzadeh et al. anticipates the instant invention as claimed.

Claims 1-6, and 15-22 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/85920 A2 (11/15/01), hereafter referred to as Banchereau et al. Banchereau et al. teaches the preparation of immature dendritic cells by culturing dendritic cell precursors in the presence of GM-CSF and IL-15, and the maturation of the dendritic cells by treatment with LPS or CD40L (Banchereau et al., pages 8m 10, 12-13 and 19). Banchereau et al. further teaches that the mature dendritic cells produced from the culture of dendritic precursors in GM-CSF and IL-15 exhibited expression of CD1a, and high levels of CD80 and CD86 (Banchereau et al., page 13 and Figure 2a). Banchereau et al. further teaches the administration of the mature IL-15 dendritic cells to a patient to induce an immune response, where the IL-15 dendritic cells have further been exposed to antigen (Banchereau et al., page 13 and page 26, claim 10). While Banchereau et al. did not do a direct comparison of the phenotype of the IL-15 dendritic cells with dendritic cells produced from cultures in GM-CSF and IL-4, it is noted that the IL-15 dendritic cells of Banchereau et al. were produced using the same culture conditions, i.e. culture in IL-15 and GM-CSF, and appear to express the same markers. It is also noted that while Banchereau et al. did not test the ability of these cells to induce the proliferation or activation of NK cells, "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). Further, the applicant is reminded that the office does not have the facilities for examining and

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comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). Thus, by teaching mature dendritic cells produced from the culture of monocytic precursor cells in IL-15 and GM-CSF, Banchereau et al. anticipates the products as claimed.

It is further noted in reference to the methods claims, claims 15-22, that the methods as claimed contain a single method step, "contacting the NK cells with a dendritic cell". Dependent claim 19 clarifies that the "contact" can be "in vivo". Banchereau et al. teaches the *in vivo* administration of mature IL-15 dendritic cells to a mammal to induce an immune response. Mammals comprise NK cells, such that *in vivo* administration of dendritic cells constitutes contact of dendritic cells with NK cells. While Banchereau et al. teaches the stimulation of T cells, not NK cells, it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff*, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); *In re Swinehart*, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). The MPEP also states that "when the claim recites using an old composition or structure and the 'use' is directed to a result or property of that composition or structure, then the claim is anticipated. *In re May*, 574 F. 2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)". MPEP

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2112.02. As such, by teaching the same method step as the instant claimed methods, Banchereau et al. anticipates the instant methods as claimed.

Claims 1, 6, 15, and 18-21 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,849,452 (2/1/05), hereafter referred to as Zitvogel et al. Zitvogel et al. teaches methods for inducing the activation of NK cells comprising contacting resting NK cells with mature dendritic cells *in vitro* or *ex vivo* (Zitvogel et al, columns 2-3, and columns 29-30, claims 1-11). Zitvogel et al. further teaches that the NK cells and dendritic cells can be contacted *in vivo* by administering the dendritic cells to a mammal (Zitvogel et al., column 2). Zitvogel et al. further teaches that contact between the NK cell and dendritic cell can lead to the proliferation of the NK cell (Zitvogel et al., column 4 and column 16). Zitvogel et al. also teaches that the dendritic cells express IL-12, TNF-alpha, IL-15, and IFN α/β and that the NK cells can be population of leukocytes prepared by leukopheresis, or a highly enriched population of resting NK cells comprising more than 70% resting NK cells (columns 13 and 20). Thus, by teaching all the limitations of the claims as written, Zitvogel et al. anticipates the instant claims.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note

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that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'Anne M. Wehbe', with a long horizontal line extending to the right.